

We claim:

1. A method of inhibiting a phosphatidylinositol signaling cascade in a cell comprising contacting a cell expressing a phosphatidylinositol phospholipid with an effective amount of an agent comprising a chlorotoxin binding domain, wherein the chlorotoxin binding domain binds to the phosphatidylinositol phospholipid.

2. The method of claim 1 further comprising contacting the agent with a phosphatidylinositol phospholipid *in vitro* to determine the effective amount of the agent.

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3. A method of inhibiting a phosphatidylinositol signaling cascade in a cell comprising contacting a cell expressing a phosphatidylinositol phospholipid with an agent comprising a chlorotoxin binding domain, wherein the agent is not full length chlorotoxin.

15 4. The method of claim 1 wherein the agent inhibits one or more plasma membrane functions that require the phosphatidylinositol phospholipid.

5. The method of claim 4 wherein the plasma membrane function is selected from the group consisting of a membrane trafficking function, a membrane-cytoskeletal function and a cell signaling function.

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6. The method of claim 5 wherein the membrane trafficking function is selected from the group consisting of endocytosis and exocytosis.

25 7. The method of claim 4 wherein the membrane-cytoskeletal function is selected from the group consisting of microvilli formation and phagocytosis.

8. The method of claim 4 wherein the cell signaling function is selected from the group consisting of protein kinase activity, GTPase activity and EGFR-dependent membrane ruffling.

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9. The method of claim 1 wherein the inhibition of the phosphatidylinositol signaling cascade is effective for the treatment of cancer.

10. A method of inhibiting the activity of a cancer cell expressing a phosphatidylinositol phospholipid on the cell surface comprising contacting the cell with an agent comprising a chlorotoxin binding domain.

5 11. The method of claim 10 wherein the activity is cancer cell division.

12. The method of claim 10 wherein the cancer cell division is arrested at the G1/S phase of the cell cycle.

10 13. The method of claim 10 wherein the activity is the phosphotidylinositol cell signaling pathway.

14. The method of claim 10 wherein the inhibition of cancer cell activity is effective for the treatment of cancer.

15 15. A method of treating cancer in a patient in need of such treatment comprising administering an effective amount of a composition comprising an agent containing a chlorotoxin binding domain that binds to a cancer cell expressing a phosphatidylinositol phospholipid.

20 16. The method of claim 15 further comprising contacting the agent with a phosphatidylinositol phospholipid *in vitro* to determine the effective amount of the agent.

17. A method of treating cancer in a patient in need of such treatment comprising administering an effective amount of a composition comprising an agent containing a chlorotoxin
25 binding domain that binds to a cancer cell expressing a phosphatidylinositol phospholipid, wherein the agent is not full length chlorotoxin.

18. The method of claim 1, 10, 15 or 17 wherein the phosphotidylinositol phospholipid is a monophosphate.

30 19. The method of claim 18 wherein the phosphotidylinositol monophosphate is phosphatidyinositol 3-phosphate or phosphatidyinositol 4-phosphate.

20. The method of claim 1, 10, 15 or 17 wherein the phosphotidylinositol phospholipid
35 is a bisphosphate.

21. The method of claim 20 wherein the bisphosphate is phosphatidylinositol 3,4-bisphosphate or phosphatidylinositol 4,5-bisphosphate.

5 22. The method of claim 1, 10, 15 or 17 wherein the phosphotidylinositol phospholipid is a trisphosphate.

23. The method of claim 22 wherein the trisphosphate is phosphatidylinositol 3,4,5-trisphosphate.

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24. The method of claim 1, 10, 15 or 17 wherein the agent is a polypeptide.

25. The method of claim 1, 10, 15 or 17 wherein the agent comprising a chlorotoxin binding domain is chlorotoxin.

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26. The method of claim 1, 10, 15 or 17 wherein the agent is a chlorotoxin peptide mimetic.

27. The method of claim 24 wherein the polypeptide comprises at least two chlorotoxin binding domain capable of binding to a phosphotidylinositol phospholipid.

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28. The method of claim 24 wherein the polypeptide comprising a chlorotoxin binding domain comprises the amino acid sequence KGRGKCY (SEQ ID NO: 8).

25 29. The method of claim 1, 10, 15 or 17 wherein the agent is suitable for use in humans.

30. The method of claim 1, 10, 15 or 17 wherein the cancer is selected from a cancer selected from the group consisting of lung cancer, bone cancer, liver cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia,

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lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), neuroectodermal cancer, spinal axis tumors, glioma, meningioma and pituitary adenoma.

5 31. A method of identifying an agent which binds to phosphatidylinositol phospholipid comprising:

 (a) contacting the phosphatidylinositol phospholipid with the agent in the presence of a polypeptide containing a chlorotoxin binding domain, and

 (b) detecting the binding of the agent to the phosphatidylinositol phospholipid.
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 32. The method of claim 31 further comprising measuring the level of binding of the agent to the phosphatidylinositol phospholipid.

 33. The method of claim 31 wherein the method further comprises comparison to a
15 control.

 34. The method of claim 33 wherein the control is a negative control that does not contain a phosphatidylinositol phospholipid.

20 35. The method of claim 33 wherein the control is a positive control which comprises a phosphatidylinositol phospholipid contacted with chlorotoxin.

 36. The method of claim 35 wherein the chlorotoxin is labeled.

25 37. The method of claim 31 wherein the phosphatidylinositol phospholipid is expressed on the surface of cells.

 38. The method of claim 37 wherein the cells are exposed to the agent *in vitro*.

30 39. The method of claim 37 wherein the cells are eukaryotic or prokaryotic cells.

 40. The method of claim 37 further comprising measuring the level of the phosphatidylinositol phospholipid on the surface of the cells.

41. The method of claim 37 further comprising measuring differentiation or proliferation of the cells.

42. The method of claim 37 wherein the cells are cancer cells.

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43. The method of claim 37 wherein the cells are disrupted prior to contact with the agent.

44. The method of claim 31 wherein the agent is selected from the group consisting of chemical compounds, oligonucleotides, peptides and antibodies.

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45. The method of claim 31 wherein the agent is labeled.

46. The method of claim 45 further comprising measuring binding of the labeled agent to the phosphatidylinositol phospholipid.

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47. The method of claim 31 wherein the polypeptide containing a chlorotoxin binding domain is labeled.

48. The method of claim 31 wherein the polypeptide containing a chlorotoxin binding domain is chlorotoxin.

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49. The method of claim 31 wherein the polypeptide containing a chlorotoxin binding domain comprises the amino acid sequence KGRGKCY (SEQ ID NO: 8).

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50. The method of claim 31 wherein the phosphatidylinositol phospholipid is linked to a bead.

51. The method of claim 31 wherein the phosphatidylinositol phospholipid is a monophosphate.

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52. The method of claim 51 wherein the phosphatidylinositol monophosphate is phosphatidylinositol 3-phosphate or phosphatidylinositol 4-phosphate.

53. The method of claim 31 wherein the phosphatidylinositol phospholipid is a bisphosphate.

54. The method of claim 53 wherein the bisphosphate is phosphatidylinositol 3,4-
5 bisphosphate or phosphatidylinositol 4,5-bisphosphate.

55. The method of claim 31 wherein the phosphatidylinositol phospholipid is a trisphosphate.

10 56. The method of claim 55 wherein the trisphosphate is phosphatidylinositol 3,4,5-
trisphosphate.

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